Local Fibrinolysis for Middle Cerebral Artery Embolism

Criteria for the Indication by Evaluation of Residual Cerebral Blood Flow and the Results

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Summary

We summarize our clinical experience of the local fibrinolysis for the middle cerebral artery (MCA) embolism. We added residual CBF factors of the ischemic territories to the usual criteria for the indication of fibrinolysis by Xe-SPECT CBF measurement. Forty-nine cases of local fibrinolysis for MCA embolism were reviewed and the results were compared with the conservative medical treatment cases.

Angiographical improvements were achieved in 38 cases (76%, full reopening 17/49, partial reopening 21/49) and favorable outcomes (good recovery at GOS) were obtained in 32 cases (65%) at three months follow-up outcome. In comparison with the conservative medical treatment, fibrinolysis was superior at good recovery rate, severe disability rate and the resulted large infarction rate with statistical significance.

We concluded that the local fibrinolysis with evaluation of the residual CBF of the ischemic territories achieved good results and outcomes and superior to the conservative medical treatment at some points. To keep the therapeutic time window, it is necessary to include the CBF factor to the criteria for the indication of this treatment.

Introduction

Acute cerebral stroke treatment has been changed time by time along with the development of the methods of the treatment and the diagnostic equipment. Among these situation, local fibrinolysis has been playing a major role in acute cerebral stroke treatment by its high reopening rate and dramatic recovery from the stroke [1,3]. But the cases were limited by the time from the onset to treatment and the results of this treatment were not always good with falling into cerebral infarction or with hemorrhagic complication in spite of full reopening of occluded vessels in some cases [4]. What is the most important factor to perform this treatment with safe and to achieve better results? Time from the onset to treatment? or severity of the ischemia? We discussed about these questions through our clinical experience of the local fibrinolysis.

Material and Methods

Since 1990.10 to 1999.6, we have had 49 cases of local fibrinolysis for the MCA embolism. They consisted 14 females and 35 males, age from 31 to 79 year-old. Our criteria for the in-

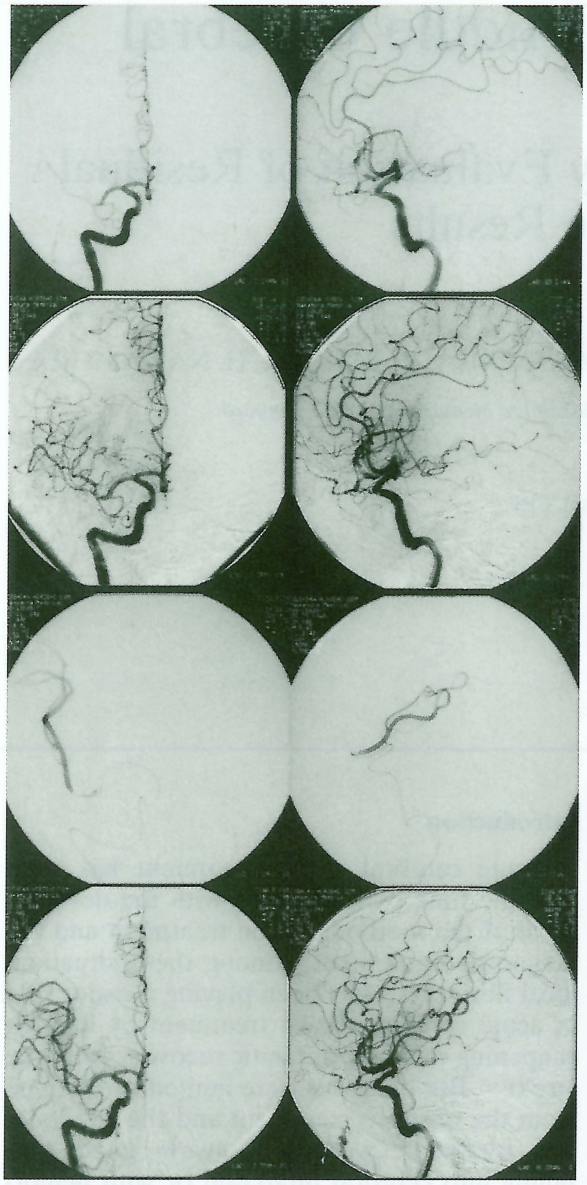

Figure 1 Angiographical summary; pre-treatment, during the treatment after the reopening of lower trunk of MCA, selected angiography through the microcatheter and post treatment.

dication of local fibrinolysis for the MCA embolism were: 1) A case of symptomatic cerebral embolism (sudden onset, association of atrial fibrillation, arrhythmia etc). 2) Within 6 hours from the onset. 3) No infarction or ischemic change at CT, MRI and/or MRI (DWI). 4) Preserving the residual cerebral blood flow (CBF) of the ischemic territory over than 15 ml / 100 g / min evaluated by 133-Xe-SPECT[5,6].

Local fibrinolysis was performed by endovascular technique using microcatheter. Usually the procedure was performed immediate after the diagnostic cerebral angiography. Using four to six French size guiding catheter, the microcatheter was navigated to the occlusion site. At the point of occlusion, the micro-guide wire passed the embolus and the tip of the microcatheter was positioned beyond the embolus position. Control angiography via the microcatheter was done using 50% diluted contrast medium to detect the position of the embolus, the length of the embolus and the distal tandem occlusion. Urokinase (UK) or rtPA was used as the fibrinolytic agents diluted 5M / 20 ml (rtPA) or 240,000 units / 20 ml (UK) and injected using the syringe pump by rate 20 ml / 15 min. Injection position was principally beyond the embolus position to keep the high concentration of fibrinolytic agents using leptomeningeal back flow from the ACA and/or PCA. Total dose of fibrinolytic agents were ranged from 5 to 15M units (rtPA) or from 240,000 to 960,000 units (UK). End point of the procedure was when the full reopening was recognized by control angiography or total dose of fibrinolytic agents reached to the upper limit (15M units at rtPA or 960,000 units in UK)[8].

Results

Angiographical Results

Angiographical results were evaluated by the cerebral angiography immediate after the local fibrinolysis. These results were categorized by 1) full reopening; total full reopening of the MCA branches, 2) partial reopening; at least one MCA trunk reopening including distal branch occlusion with full reopening of the trunk level, 3) embolus migration; embolus is migrated to distal portion of the MCA but no reopening of the MCA trunk, 4) no change; no angiographical improvement.

Angiographical results of this series were full reopening 17/49 (34.7%), partial reopening 21/49 (42.8%), embolus migration 4/49 (8.2%) and no change 7/49 (14.3%). Angiographical improvements were achieved in 17+21/49 (77.6%).

Three months follow-up outcome

Clinical outcome of this series were evaluated by Glasgow Outcome Scale at three months follow-up. The results were good recovery 32/49

(65.3%), moderate disability 10/49 (20.4%), severe disability 3/49 (6.1%), persistent vegetative state 0/49 (0%) and death 4/49 (8.2%).

Consevative medical therapy group

To compare the clinical results of local fibrinolysis, we summarized 39 cases who were treated with conservative medical therapy. These were the cases who were treated before the introduction of local fibrinolysis or local fibrinolysis was not performed because of age, general condition and accessibility of angiocatheter. They consisted 16 females and 23 males, age from 36 to 89 year-old. In these cases, age, gender, side of the occlusion, time from the onset to angiography (within 6 hours), residual CBF of the ischemic territory (over than 15ml / 100g/min evaluated by 133-Xe-SPECT) were matched. There was no statistical significance about these factors between local fibrinolysis group and conservative medical therapy group. Three months follow-up outcome of these group evaluated by GOS results were good recovery 12/39 (30.8%), moderate disability 8/39 (20.5%), severe disability 16/39 (41.0%), persistent vegetative state 0/39 (0%) and death 3/39 (7.7%).

Comparing with local fibrinolysis and conservative medical therapy

We compared the infarction size, severity of hemorrhagic infarction and three months follow-up outcome (table 1, 3). There was a statistical significance at large infarction rate ($p<0.0001$, double KAI test), good recovery rate ($p=0.008$ double KAI test) and severe disability rate ($p<0.0001$ double KAI test).

Representative case report

A case of 50 year-old male with sudden onset of the left hemiparesis and dysarthria transferred 1 hour after the onset. Cerebral angiography demonstrated the right middle cerebral artery occlusion at the M1 distal portion. No infarction on CT and MRI and no ischemic change at DWI. Residual CBF of the ischemic territories were 26 ml / 100 g/min on 133 Xe-SPECT. Immediately after the diagnostic angiography, we performed local fibrinolysis using Urokinase. After the administration of 960,000 units of U.K., angiographical full reopening was achieved and the patient recovered from the symptoms. CBF of the ischemic territories were improved to 34 ml / 100 g/min after the treatment. Small cerebral infarction was appeared at the right caudate head on MRI but the patient had no neurological deficit at the discharge (figures 1, 2).

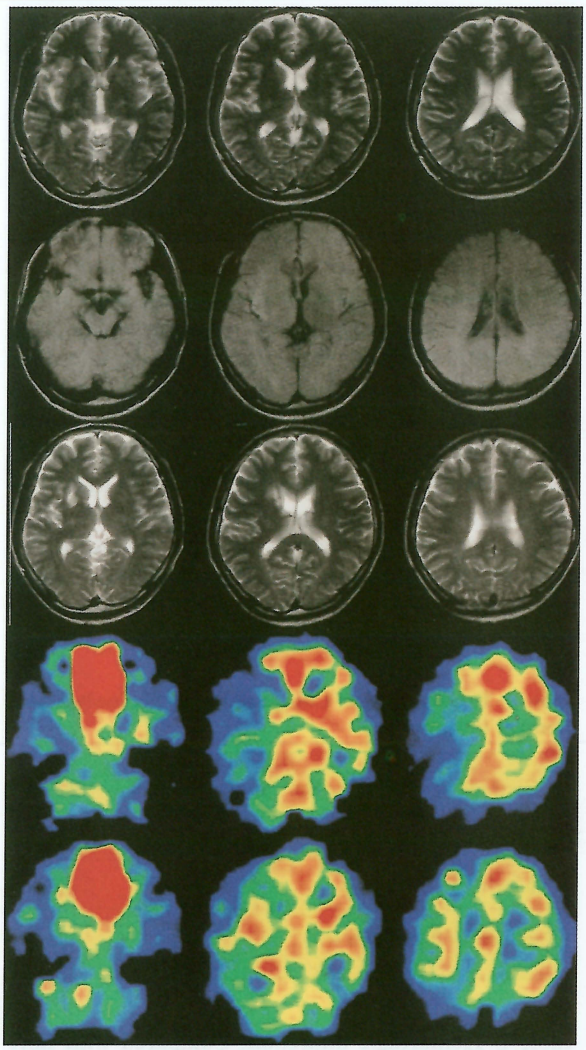

Figure 2 MRI and Xe-SPECT; T2WI and DWI on admission, T2WI at discharge, 133Xe-SPECT pre-fibrinolysis and post fibrinolysis.

Discussion

In acute cerebral stroke, the priciple of the treatment is a recovery from the ischemia before the brain falling into the infarction. Therapeutic time window of the acute cerebral

stroke depends on various factors such as patient condition, residual CBF of the ischemic territories and the site of the occlusion etc. Classical golden time, 6 hours, is coming from our experience in acute stroke management that means no cerebral infarction on CT scan within 6 hours. With the development of neuroimaging tool such as MRI especially DWI at MRI, [9,10] the time from the onset to falling into the cerebral infarction is changing. As the sensitivity of the ischemic change increased, we could detect the cerebral infarction or cerebral ischemic change earlier than 6 hours. Early ischemic change detected by MRI-DWI is deeply related both residual CBF of the ischemic territories and the time from the onset to MRI examination [12]. We use the value of residual CBF of the ischemic territories for the inclusion criteria of this treatment. Residual CBF is also recognized as an important factor in this treatment to achieve good recovery from the ischemia and to avoid severe hemorrhagic complication [8,11].

We could not perform this treatment for every patient as soon as the patient had stroke. It needed the time for transportation, for CT, MRI examination, for CBF study and for cerebral angiography. So we decided therapeutic time window and treat the patient within this time window under the condition that the patient is reversible state from the ischemia. To measure the residual CBF and limit the candidate by residual CBF means to keep this therapeutic time window. And we thought it might be supplementary by MRI-DWI from our recent experience [12].

Worst results of this treatment were found in patient with poor angiographical results. To achieve the better results, it is necessary to do additional treatment for these patients. Direct PTA without using fibrinolytic agents is one of the another method but the accessibility of the balloon catheter is a great problem [7]. Prior tPA intravenous administration and combination of this treatment may increase the reopening rate. Recent clinical trial reports this combination provides better recanalization but resulted relatively high incidence of hemorrhagic infarction [13]. We recently introduced new additional treatment for non-reopening patient without high dose of fibrinolytic agents and easy to access. It was "Soft Balloon Angioplasty" using very soft silicone balloon catheter used at the balloon angioplasty for cerebral vasospasm. Using a micro-guide wire inside the balloon catheter, it is relatively easy to access to the non-reopening area, and the balloon breaks the embolus with a few times of delicate inflation. The embolus seems to be frangible by prior administration of fibrinolytic agents. This technique may be a great help for the increasing the reopening rate and achieve better results.

Table 1 **Infarction size; Compared with fibrinolysis and medical therapy**

Infarction size	No infarction	Small	Medium	Large*
Fibrinolysis	7	22	15	5
Medical	2	10	7	20

** p<0.0001 (double KAI test)*

Table 2 **Hemorragic infarction; Compared with fibrinolysis and medical therapy**

	None	Local	Partial	Extensive
Fibrinolysis	38	6	3	2
Medical	23	2	9	5

Table 3 **Glasgow Outcome Scale at three months follow-up; Compared with fibrinolysis and medical therapy**

GOS	GR*	MD	SD**	PVS	D
Fibrinolysis	32	10	3	0	4
Medical	12	8	16	0	3

** p=0.0008; ** p<0.0001 (double KAI test)*

Conclusions

Fibrinolysis for MCA embolism with evaluation of residual CBF could achieve angiographical and clinical improvements. And it is superior to the conservative medical therapy group in some points. Limitation of candidates by residual CBF could keep a certain therapeutic time window and could achieve good results in two third of the patients.

References

1 Freitag HJ, Becker VU et Al: Local fibrinolytic therapy for acute embolic stroke. Advantages due to Lys-plasminogen. In: Taki W, Picard L, Kikuchi H (eds): Advances in Interventional Neuroradiology and Intravascular Neurosurgery. Elsevier, Amsterdam 1996: 441-446.

2 Schumacher M, Siekmann R et Al: Intra-arterial fibrinolitic therapy in acute cerebral artery occlusion. In: Taki W, Picard L, Kikuchi H (eds): Advances in Interventional Neuroradiology and Intravascular Neurosurgery. Elsevier, Amsterdam 1996: 447-452.

3 Higashida RT, Halbach et Al: Thrombolytic therapy in acute stroke. In: Taki W, Picard L, Kikuchi H (eds): Advances in Interventional Neuroradiology and Intravascular Neurosurgery. Elsevier, Amsterdam 1996: 453-457.

4 Komiyama M, Nishikawa M et Al: Local fibrinolysis for cardioembolic occlusion of the internal carotid artery. In: Taki W, Picard L, Kikuchi H (eds) Advances in Interventional Neuroradiology and Intravascular Neurosurgery. Elsevier, Amsterdam 1996: 463-467.

5 Hyogo T, Kataoka T et Al: Endovascular thrombolytic therapy for MCA embolism. In: Taki W, Picard L, Kikuchi H (eds) Advances in Interventional Neuroradiology and Intravascular Neurosurgery. Elsevier, Amsterdam 1996: 469-471.

6 Ueda T, Ohta S et Al: Relationship between residual CBF and neurological outcome in thrombolytic therapy. In: Taki W, Picard L, Kikuchi H (eds) Advances in Interventional Neuroradiology and Intravascular Neurosurgery; Elsevier, Amsterdam 1996: 487-490.

7 Uno J: Direct PTA for acute ischemic stroke. Interventional Neuroradiology 3 (suppl 2): 47-50, 1997.

8 Hyogo T, Kataoka T et Al: Thrombolytic therapy for cerebral embolism. Interventional Neuroradiology 4 (suppl 1): 23-25, 1998.

9 Warach S: New MR technologies for diagnosis of acute ischemic stroke: MR angiography, Diffusion, and perfusion images. In: Yamaguchi T, Mori E et Al (eds) Thrombolytic Therapy in Acute Ischemic Stroke III; Springer-Verlag, Tokyo 1995: 81-85.

10 Fisher M: Application of diffusion-weighted magnetic resonance imaging for stroke diagnosis and treatment. In: Yamaguchi T, Mori E et Al (eds): Thrombolytic Therapy in Acute Ischemic Stroke III; Springer-Verlag, Tokyo 1995: 115-123.

11 Hyogo T: Ischemic Cerebral Stroke, Thrombolytic Therapy. Clinical Neuroscience 16 (6): 661-663, 1998.

12 Yoshida H, Nakagawara J, Hyogo T: Cortical hyperintensity area on DWI depends on both residual CBF and time from the onset in acute cerebral ischemia. Jpn J Stroke 20: 567-572, 1998.

13 Christopher AL, Frankel M et Al: Combined intravenous and intra-arterial therapy of acute ischemic stroke. Stroke 30: 2598-2605, 1999.

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